In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 18-1522V
Filed: May 8, 2024

ERIN M. KINNEY,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Phyllis Widman, Widman Law Firm, LLC, Northfield, NJ, for petitioner.
Neil Bhargava, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On October 2, 2018, petitioner filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012) ("Vaccine Act").[2] (ECF No. 1.) Petitioner initially alleged that she suffered a seizure disorder, postural orthostatic tachycardia syndrome ("POTS"), and fibromyalgia following the administration of an influenza ("flu") vaccine on October 15, 2015, and a measles-mumps-rubella ("MMR") vaccine on October 21, 2015. (*Id.*) Petitioner later amended her petition to allege that the flu and MMR vaccines caused her to suffer "a seizure disorder/epilepsy, periodic paralysis, syncope, exacerbation of migraines, [POTS], cataplexy, narcolepsy, fibromyalgia, focal postganglionic sudomotor impairment chronic fatigue, and severe anxiety and depression." (ECF No. 38.) For the reasons set forth below, I conclude that petitioner is *not* entitled to compensation for her injuries.

[1] Because this document contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] Within this decision, all citation to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991). Because petitioner's injuries are not listed on the Vaccine Injury Table, petitioner must satisfy this burden of proof.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based

solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine.

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. However, that expert's opinion must be based upon "sound and reliable" scientific explanation. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (quoting *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs*., 35 F.3d 543, 548-49 (Fed. Cir. 1994)). The *Althen* court also indicated that, in finding causation, a Program factfinder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." 418 F.3d at 1280.

II. Procedural History

This case was initially assigned to Special Master Moran. (ECF No. 4.) Petitioner filed initial medical records as well as several witness affidavits in support of her claim. (ECF Nos. 9, 12.) This case was reassigned to my docket on August 27, 2019. (ECF No. 25.) Petitioner then filed additional witness affidavits. (ECF No. 28.) After reviewing petitioner's filings, respondent filed his Rule 4(c) report recommending against compensation on November 4, 2019. (ECF No. 31.) Subsequently, petitioner filed additional medical records in November 2019 and January 2020. (ECF Nos. 32, 36.)

On January 7, 2020, petitioner filed her amended petition adding additional conditions to her allegations. (ECF No. 38.) Petitioner then filed an expert report from Yuval Shafrir, M.D., on April 4, 2020. (ECF No. 41; Ex. 25.) Petitioner also filed further medical records in April and May of 2020. (ECF Nos. 49, 50.) On July 22, 2020, petitioner filed a supplemental report from Dr. Shafrir incorporating a discussion of the recently filed medical records. (ECF No. 52; Ex. 93.) Respondent subsequently filed a

responsive expert report from M. Steven Evans, M.D., on November 3, 2020. (ECF No. 56; Ex. A.)

Petitioner again filed additional treatment records in December 2020 and February 2021 (ECF Nos. 63, 65), followed by a second supplemental expert report from Dr. Shafrir on May 27, 2021 (ECF No. 70; Ex. 98). Petitioner then filed additional records on June 2, 2021. (ECF No. 72.) On August 30, 2021, the exchange of expert reports concluded with respondent's filing of a supplemental report from Dr. Evans. (ECF No. 75; Ex. C.) Following the exchange of expert reports, petitioner requested that this case be set for a hearing. (ECF No. 77.)

In anticipation of the hearing, petitioner filed additional evidence in January 2023, including updated medical records and a supplemental affidavit. (ECF No. 89.) The parties then filed a joint prehearing submission outlining the stipulated facts and facts in dispute on January 24, 2023. (ECF No. 93.) On February 14, 2023, the parties filed simultaneous prehearing briefs. (ECF Nos. 98, 99.) Respondent also filed a summary of the medical literature contemporaneous with his prehearing brief. (ECF No. 99-1.) Petitioner then filed a reply brief on February 22, 2023, followed by a summary of the medical literature on February 28, 2023. (ECF Nos. 101, 104.)

An entitlement hearing was held on March 7, 2023. Petitioner, Dr. Shafrir, and Dr. Evans, testified. (*See* Transcript "Tr." at ECF No. 109.) At the close of the hearing, both parties confirmed that post-hearing briefs were unnecessary. (Tr. 224.) This case is now ripe for resolution.

III. Factual History

a. As Reflected in the Medical Records

Prior to vaccination, petitioner's medical history was significant for migraines, fibroadenoma of the breast, urinary tract infection, and pyelonephritis. (Ex. 6, pp. 13-19, 77, 92, 149-51; Ex. 91, pp. 12-14.) Petitioner received a flu vaccination on October 15, 2015, and an MMR vaccine on October 21, 2015. (Ex. 1; Ex. 2, ¶ 2; Ex. 6, pp. 142-43.)

On November 24, 2015, petitioner saw Dr. Jessica McCool who reported that petitioner was experiencing dizzy spells, during which petitioner "experiences tachycardia and feels like she can't catch her breath." (Ex. 95, p. 10.) Petitioner's labs from this visit came back as normal. (Ex. 6, p. 512.) Petitioner underwent a twenty-four-hour Holter monitor for tachycardia on December 1, 2015. (*Id.* at 191-92.) The monitor revealed sinus rhythm with low grade ventricular ectopy, brief early morning ectopic atrial bradycardia, and no correlation of any specific rhythm disturbance or ST changes with symptoms. (*Id* at 192.) Petitioner saw Dr. McCool again on December 17, 2015. (Ex. 95, p. 19.) Dr. McCool reported that petitioner's sleep studies showed "no abnormalities." (*Id.*) Petitioner reported that "she has had [two] episodes where she wakes up and cannot move her legs," for about an hour. (*Id.*) Additionally, petitioner reported falling asleep in the middle of doing something else. (*Id.*) Dr. McCool

explained that "[b]ased on her current symptoms, [she] believe[d] that [petitioner] could be suffering from narcolepsy with cataplexy." (*Id.* at 20.)

On December 21, 2015, petitioner visited pulmonologist Jorge Alvarez, M.D. at the Jennie Edmundson Hospital Sleep Disorder Center. (Ex. 6, p. 475.) Petitioner indicated that "thinking, stress, outside noises, anything" made her unable to fall asleep, and that this had been a problem for "4-5 years." (*Id.* at 470.) Dr. Alvarez reported that, based on petitioner's sleep study, her "sleepy efficiency was normal," however, her "REM latency was slightly prolonged," and she had a "diminished percent stage of total REM sleep." (*Id.* at 475.) On the same day, petitioner underwent a multiple sleep latency test which showed a mean sleep latency of 7.9 minutes, evidence of three REM sleep episodes, and was "consistent with and c[ould] help support a diagnosis of narcolepsy." (*Id.* at 476.) Dr. Alvarez ordered genetic testing on January 20, 2016, which was negative for the HLA-DQB1*06:02 allele, a gene strongly associated with narcolepsy. (*Id.* at 118-21.) On the same day, petitioner saw Dr. Alvarez for "excessive daytime sleepiness, possible narcolepsy." (Ex. 89, p. 7.) Dr. Alvarez reported that petitioner "apparently had a [flu] vaccination this past year." (*Id.*) Her symptoms included "[e]xcessive daytime sleepiness intermittently throughout the day." (*Id.*) Dr. Alvarez recorded petitioner's impression as narcolepsy with cataplexy and anxiety. (*Id.* at 7-8.)

Petitioner's next follow up appointment with Dr. Alvarez for possible narcolepsy with cataplexy was on February 22, 2016. (Ex. 89, p. 5.) Petitioner reported sleeping eight hours a night, however, not feeling rested. (*Id.*) She reported repetitive movements, but no seizure activity. (*Id.*) Dr. Alvarez assessed petitioner with fear and anxiety; repetitive words and movements, possible neurologic seizures; arthralgias; and a working diagnosis of narcolepsy with cataplexy. (*Id.*) Petitioner was prescribed a low dose of Xyrem. (*Id.* at 6.) On February 25, 2016, petitioner saw Dr. McCool for a follow up appointment regarding her narcolepsy diagnosis. (Ex. 95, p. 13.) She complained of the following symptoms: "word finding difficulty, worsening headaches, a problem with her depth perception (no recent eye exam), episodes of confusion, muscle twitching, joint pain distally (hands and feet, although no joint swelling), and her feet appearing purplish in color at times." (*Id.*) Petitioner reported feeling depressed about her diagnosis. (*Id.*)

On March 15, 2016, petitioner had an appointment with Joseph F. Shehan, M.D an internist. (Ex. 7, pp. 71-73.) Petitioner reported that around November 5, 2015, she "started getting an unusual syndrome, which started with severe vertigo, nausea, progressed to headaches, progressed to narcolepsy, which progressed to cataplexy spells." (*Id.* at 71.) Petitioner stated that she had now developed numbness and tingling in her hands, arm weakness, and bilateral headaches that would start in the back of the head. (*Id.*) She also noted that she had sustained numerous falls and has woken up on the ground with no recollection of what happened. (*Id.*) Petitioner informed Dr. Shehan that she had received flu and MMR vaccines in October 2015. (*Id.*) Dr. Shehan noted that petitioner "has an unusual syndrome complex and this may relate to immunizations." (*Id.* at 73.) He added, "I am going to have to research [the

vaccines] a little bit to see if there is anything that makes sense." (*Id.*) Dr. Shehan ordered a brain MRI, which petitioner underwent on March 19, 2016. (Ex. 4, pp. 167-68.) The MRI showed mild scattered, punctate, nonspecific cerebral white matter signal of unknown acute or ongoing significance, but no acute infarct, mass effect, or evidence of acute intracranial hemorrhage. (*Id.* at 167.)

Petitioner presented to neurologist John Puente, M.D., on March 31, 2016. (Ex. 5, pp. 4-5.) Petitioner reported that she was in good health until around November 2015, when she "had an episode while at a convention where she thought she was food poisoned" and "was bedridden and nauseous with vertigo for longer than a day." (*Id.* at 4.) Petitioner further informed Dr. Puente that "she has had episodes of weakness, but also falling episodes." (*Id.*) Additionally, petitioner reported having "pain mostly in joints and finally anxiousness." (*Id.*) Petitioner also noted that she had symptoms of intermittent weakness, worse on the right side; episodes of her legs "go[ing] out;" and episodes of dizziness and vertigo followed by falling asleep or confusion. (*Id.*) Dr. Puente noted that petitioner was diagnosed with narcolepsy following an abnormal sleep study but that the bloodwork was inconclusive. (*Id.*) He further noted that petitioner's brain MRI revealed non-specific findings. (*Id.*) Dr. Puente ordered an EMG to investigate weakness and an EEG to investigate potential seizures and recommended petitioner consult a sleep specialist and pursue more aggressive migraine therapy. (*Id.* at 5.) Later that day, petitioner followed up with Dr. Shehan and reported feeling better. (Ex. 7, p. 68.) Petitioner stated that her general wellbeing had improved with Lexapro. (*Id.*) Her neurologic examination was normal. (*Id.* at 69.) Dr. Shehan noted that petitioner had received the MMR and flu shot in October of 2015, and then developed severe vertigo on November 5, 2015, which was "[f]ollowed by [n]arcolepsy progressing to [c]ataplexy." (*Id.* at 70.) Petitioner was started on proprandolol for her migraines. (*Id.*)

Petitioner presented to Jonathon Moravek, M.D., on April 18, 2016 for an EMG and nerve conduction study ("NCS") to evaluate her intermittent weakness and pain in her ankles and wrists. (Ex. 5, pp. 6-9.) The EMG/NCS was normal. (*Id.* at 8-9.) Then, petitioner presented to John Bertoni, M.D., on April 27, 2016, for a video EEG, which was also normal. (*Id.* at 16-18.) On May 12, 2016, petitioner returned to Dr. Puente, who noted that propranolol "seems to have helped" her migraine prophylaxis. (*Id.* at 10.) Dr. Puente recommended petitioner consult with a sleep specialist. (*Id.*)

Petitioner followed up with Dr. Shehan on June 7, 2016. (Ex. 7, pp. 65-67.) Dr. Shehan noted that petitioner "presented today basically with a litany of different issues," including "increasing migraines, increasing spells which have been described as cataplexy and narcolepsy," and explained that the etiology of these conditions "remains uncertain." (*Id.*) Dr. Shehan documented two different types of spells petitioner was experiencing, including "what is sort of an expressive aphasia." (*Id.*) Dr. Shehan referred petitioner to Barbara Clinkenbeard, APRN, for a second opinion. (*Id.* at 67.)

On July 11, 2016, petitioner returned to Dr. Shehan for continuing spells. (Ex. 7, pp. 62-64.) Dr. Shehan prescribed Adderall and referred petitioner to pulmonary

disease specialist John Shehan, M.D.[3], and neurologist Bernadette Hughes, M.D., for evaluation for her spells. (*Id.* at 64.) Petitioner had an appointment with Dr. Hughes on July 18, 2016, with a chief complaint of "dizziness and falling, migraines with nausea." (Ex. 23, p. 1.) Petitioner explained that she had experienced headaches since she was 14. (*Id.*) However, in November of 2015, those headaches increased, lasted two or three days and she began to experience spells. (*Id.* at 1-2.) Petitioner was then diagnosed with narcolepsy and cataplexy. (*Id.* at 2.) Petitioner reported that her neurological tests had come back negative. (*Id.*) Dr. Hughes recommended seeing a psychotherapist for cognitive behavior therapy. (*Id.* at 4.)

Petitioner presented to Nurse Clinkenbeard on July 20, 2016. (Ex. 7, pp. 60-61, 90-91.) She diagnosed petitioner with generalized anxiety disorder, panic attacks and major depression. (*Id.* at 60.) Petitioner reported that she experienced her first depressive episode in January 2016. (*Id.* at 90.) Nurse Clinkenbeard noted that petitioner was easily overstimulated and angry, that she had an illogical thought process at times, that she had thought blocking, that her abstract reasoning was impaired, and that her judgment and insight were moderately impaired. (*Id.* at 90-91.) Petitioner told Nurse Clinkenbeard that she had a three-day migraine in November 2015, followed by an increased frequency of migraines and episodes of falling asleep and falling. (*Id.* at 91.) Nurse Clinkenbeard referred petitioner to therapist Jessica Winternheimer. (*Id.*)

On August 29, 2016, petitioner presented to Dr. Puente and reported that her migraines were less severe but still frequent during the summer, which "limited her activity level at times." (Ex. 5, p. 12.) Petitioner noted that she was interested in pursuing acupuncture and herbal and non-traditional therapies. (*Id.*) Dr. Puente recommended petitioner try acupuncture, feverfew, magnesium, and a riboflavin supplement. (*Id.*) Petitioner returned to Nurse Clinkenbeard on August 31, 2016. (Ex. 7, pp. 58-59, 92-93.) Nurse Clinkenbeard noted that petitioner was nonfunctional due to her anxiety, and questioned whether petitioner had a somatization disorder. (*Id.* at 93.) Petitioner reported blacking out in stressful situations. (*Id.*) Petitioner had a follow up appointment with internist Dr. Shehan on September 3, 2016, and reported cataplexy spells and periodic paralysis, "which may or may not be related to potassium." (*Id.* at 53.) Dr. Shehan explained that petitioner "continues to have spells," which he attributed to anxiety. (*Id.*)

Petitioner's next appointment was with Nurse Clinkenbeard on October 12, 2016. (Ex. 7, pp. 51-52, 94-95.) Petitioner reported that her mood fluctuates "more than [one to two] times per day." (*Id.* at 95.) Petitioner then underwent cognitive behavior therapy with Jessica Winternheimer between October 13, 2016, and December 22, 2016. (Ex. 19.) Petitioner reported that, "in October 2015 she began experience[ing] dizziness, 'seizures,' phantom pains and dropping things." (*Id.* at 3.) Because of these experiences, she developed anxiety. (*Id.*) Petitioner was diagnosed with generalized anxiety disorder. (*Id.* at 4.)

[3] Petitioner saw two Dr. Shehans during the course of her treatment: Dr. Joseph Shehan, an internist, and Dr. John Shehan, a pulmonologist.

On November 28, 2016, petitioner had an appointment with Dr. Puente, during which she reported that her migraines remained the same, and that she experienced a stutter, odor sensitivity, confusion after blackouts, bowel pain, and nausea. (Ex. 5, p. 14.) Dr. Puente ordered an MRI and recommended that petitioner consider going to acupuncture. (*Id.* at 15.) Petitioner had a follow up appointment with Nurse Clinkenbeard on December 12, 2016. (Ex. 7, pp. 49-50, 96-97.) Petitioner reported to internist Dr. Shehan the next day. (*Id.* at 44-48.) Dr. Shehan opined that he was "somewhat reluctant to believe these are pseudoseizures as she has lost urine incontinence [*sic*]." (*Id.* at 44.) He referred her to another neurologist, Deepak Madhavan, M.D. (*Id.* at 47.)

Petitioner presented to internist Dr. Shehan again on January 23, 2017. (Ex. 7, pp. 38-40.) During the exam, petitioner "laps[ed] into a stupor off and on," and it became "somewhat difficult to communicate with her." (*Id.* at 38.) He reported that petitioner was "fatigued, weak, and c[ould not] seem to stay on task." (*Id.*) Petitioner underwent two psychological evaluations performed by Aveva Shukert, Ph.D; one on January 30, 2017 and the second on February 6, 2017. (Ex. 17.) Petitioner "reported cataplexy-like episodes which began in November 2015." (*Id.* at 5.) She stated that it occurred after she received two vaccinations on the same day, one for MMR and one for flu vaccine." (*Id.*) Petitioner had been diagnosed with narcolepsy, however, did not agree that that diagnosis was appropriate. (*Id.*) Petitioner explained that her episodes were "triggered by sudden loud noises or stressful days." (*Id.*) Additionally, petitioner noted that she "had a history of migraines." (*Id.*) Petitioner's boyfriend explained that "he can predict when she is about to have one because she has hand tremors and stops doing the activity in which she had been engaged." (*Id.*) Dr. Shukert reported that "[t]he present evaluation was scheduled to evaluate both cognitive issues and emotional and personality issues that might have an impact on [petitioner's] episodes." (*Id.*) The first cognitive test showed that petitioner's Processing Speed Index score was below average, and she "had trouble with immediate short-term memory for visual material and building speed on this timed test." (*Id.* at 6.) Petitioner's second evaluation revealed "various negative emotional experiences and [that she] tends to be quite self-critical and guilt prone." (*Id.*) Dr. Shukert reported that petitioner reported feeling "overwhelmed by life," and that she was "prone to suicidal ideation." (*Id.* at 7.) Dr. Shukert cautioned that petitioner had been sitting with her boyfriend while completing this second exam, and that petitioner "was cautioned repeatedly not to consult him when choosing her answers." (*Id.* at 6.) Dr. Shukert's diagnostic considerations included anxiety related disorders and she recommended psychotherapy and antidepressant/antianxiety medication. (*Id.* at 7.)

On February 8, 2017, petitioner saw John C. Goldner, M.D. (Ex. 24, p. 14-16.) Dr. Goldner noted that petitioner had been diagnosed with multiple issues including, narcolepsy, weakness in her left arm of uncertain etiology, and migraines. (*Id.* at 14.) Dr. Goldner recounted how petitioner had a history of migraines that got worse after November 2015. (*Id.* at 14-15.) Additionally, petitioner described spells where she loses consciousness. (*Id.*) Dr. Goldner explained that these spells sounded like "hypnagogic hallucinations." (*Id.* at 15.) Petitioner also explained that "her wrists and

hands started to hurt, and she had trouble grasping things." (*Id.*) Dr. Goldner ordered a nerve condition study which petitioner underwent on April 6, 2017; the results of which were normal. (*Id.* at 5.)

Petitioner had an appointment with neurologist John M. Hannam, M.D. on April 11, 2017. (Ex. 4, pp. 148-51.) Petitioner reported that she had experienced migraines since she was 13 years old. (*Id.* at 148.) She explained that her migraines got worse after she developed "a flu-like illness" in November of 2015. (*Id.*) At the same time, petitioner also began to have "spells where she would suddenly collapse." (*Id.*) Before petitioner's spells, she experiences tremors which sometimes continue after she has collapsed, however, "[s]he has never had a convulsive seizure." (*Id.*) Sometimes, petitioner loses control of her bladder during these spells. (*Id.*) These spells increased when petitioner was experiencing stress or feeling depressed. (*Id.*) Dr. Hannam reported that petitioner's studies had come back as normal, except for petitioner's sleep study, which showed narcolepsy. (*Id.* at 148-49.) Dr. Hannam summarized that one of petitioner's practitioners from psychiatry suspected pseudoseizures, however, Dr. Shehan believed she could have epilepsy because she lost control of her bladder. (*Id.* at 149.) Petitioner's next follow up appointment was with internist Dr. Shehan on April 24, 2017. (Ex. 7, p. 33-35.) Dr. Shehan reported that he continued petitioner on her current course of treatment. (*Id.* at 35.) On July 18, 2017, petitioner saw internist Dr. Shehan again for migraine management. (*Id.* at 29-32.) Additionally, petitioner reported continuing to have spells. (*Id.*)

Petitioner had an initial consultation at an epilepsy clinic on September 28, 2017, with Dr. Madhavan and Erin L. Smith, M.D. (Ex. 4, pp. 151-57.) Petitioner reported that her history included migraines, narcolepsy, anxiety, and depression. (*Id.* at 152.) She again explained that her symptoms began after a flu-like illness in November of 2015. (*Id.*) Petitioner explained that she has three types of spells. (*Id.*) During one type of spell, she "seems to suddenly fall asleep and then collapse[s] to the ground." (*Id.*) During these spells, she sometimes loses incontinence. (*Id.*) Dr. Madhavan and Dr. Smith explained that these spells are consistent with narcolepsy for which she is being treated. (*Id.*) During the second type of spell, petitioner "suddenly collapse[s] to the ground, however, her eyes remain open and she appears to maintain consciousness." (*Id.*) This spell depends on petitioner's stress levels. (*Id.*) Additionally, after these spells, petitioner feels fearful and speaks like a toddler. (*Id.*) During the final type of spell, petitioner "will suddenly have a blank stare and will be able to speak, however, she requires repeated instruction and guidance to be able to function." (*Id.*) Petitioner's triggers include bright lights, reflections, and stress. (*Id.*) Dr. Madhavan and Dr. Smith scheduled petitioner for an EEG. (*Id.* at 156.)

Petitioner saw internist Dr. Shehan two more times before the end of the year, once on October 12, 2017, and then again on December 12, 2017. (Ex. 7, pp. 19-28.) On October 12, 2017, Dr. Shehan explained that some of petitioner's symptoms could be related to "a conversion disorder." (*Id.* at 24.) Dr. Shehan reported that they were waiting on the results of petitioner's EEG. (*Id.*) Petitioner reported feeling depressed. (*Id.*) Dr. Shehan prescribed cognitive therapy. (*Id.* at 27.) On December 12, 2017,

petitioner reported that her symptoms continued. (*Id.* at 19.) Dr. Shehan considered whether petitioner might have fibromyalgia. (*Id.* at 22.)

In January 2018, petitioner began seeing rheumatologist Harry Klein, M.D. (Ex. 7, pp. 14-18.) Petitioner's presenting symptoms included joint pain in her hands, ankles, and muscles, along with anxiety. (*Id.* at 14.) Petitioner explained that nine days after she received both the flu and MMR vaccines, petitioner developed flu like symptoms, her joint pain began, and her "feet also started turning purple." (*Id.*) Additionally, petitioner reported her narcolepsy diagnosis, and that her genetic testing revealed no genetic mutation for this. (*Id.*) Petitioner also reports vertigo, nausea, and headaches. (*Id.*) Dr. Klein notes that petitioner "attributes this to having had a flu shot and MMR at that time," however, he explained that after reviewing her labs he does not believe that her condition suggests an inflammatory or autoimmune process. (*Id.* at 17.) Instead, he attributes her headaches, IBS issues, and the joint pain to fibromyalgia. (*Id.*) Petitioner had a follow up appointment with internist Dr. Shehan on January 23, 2018, during which she reported that she was unable to get out of bed because of her fatigue and headaches. (*Id.* at 10.) Dr. Shehan suggested that petitioner undergo a tilt table to test for an autonomic issue like POTS. (*Id.*)

On February 5, 2018, petitioner was admitted for a long-term video EEG. (Ex. 4, p. 10.) The overnight results of this study were normal; therefore, the EEG was continued into the next day. (*Id.* at 17.) Petitioner "had one brief seizure (lasted about 20 seconds)," during the second day of her study. (*Id.* at 19.) Petitioner was discharged on February 8, 2018. (*Id.* at 20.) In the discharge summary, Dr. Madhavan reported that petitioner had a "history of migraines, narcolepsy, anxiety, depression, and of spells." (*Id.* at 21.) Dr. Madhavan reported that the "EEG monitoring study is consistent with the presence of mild to moderate diffuse cerebral dysfunction with frequent bursts of sharply contoured slowing noted diffusely." (*Id.* at 26.) Additionally, petitioner "did show onset of rhythmic activity in the fronto-central head region which appeared to be consistent with seizure." (*Id.*) One week later, petitioner had an appointment with Antonio P. Reyes, M.D. for lightheadedness. (Ex. 3, p. 3.) Petitioner reported that over the past two years she "would get sudden tachycardia" while "sitting on her couch or doing mild activities." (*Id.*) "Based on her orthostatic BP check," Dr. Reyes diagnosed petitioner with POTS and recommended increasing her fluid and salt intake and losing weight. (*Id.* at 6.) Additionally, petitioner was scheduled for an echocardiogram and a stress test. (*Id.*)

Petitioner had a follow up appointment with internist Dr. Shehan on May 7, 2018. (Ex. 7, pp. 7-9.) Dr. Shehan reported that petitioner's ongoing issues included a skin rash, fibromyalgia, unconfirmed POTS, and tachycardia. (*Id.* at 7.) Petitioner described fewer spells since increasing her potassium. (*Id.*) Petitioner was referred to another cardiologist to confirm her POTS diagnosis. (*Id.* at 9.) Petitioner reported an improvement in her symptoms to Dr. Madhavan on July 2, 2018. (Ex. 4, pp. 157-62.) On October 2, 2018, petitioner had another follow up appointment with internist Dr. Shehan. (Ex. 7, pp. 3-6.) Petitioner reported feeling much better. (*Id.* at 3.) In addition

to her current symptoms, petitioner reported a gluten intolerance and that she continues to follow a gluten free diet. (*Id.* at 6.)

In May of 2019, petitioner had her first appointment with neurologist and epileptologist Aditya Vuppala, M.B.B.S at an epilepsy clinic. (Ex. 22, pp. 162-67.) Dr. Vuppala reported that petitioner's history included migraines, narcolepsy, anxiety, depression, and seizures. (*Id.* at 162.) Petitioner explained episodes where she loses awareness once or twice a week, however, these episodes had decreased in frequency. (*Id.* at 163.) Additionally, petitioner reported falling due to her narcolepsy zero to four times a week. (*Id.*) Dr. Vuppala determined that it was possible that petitioner's episodes were epileptic seizures, however, she also notes a differential diagnosis of autonomic dysfunction. (*Id.* at 166-67.) Dr. Vuppala encouraged petitioner undergo POTS testing. (*Id.* at 167.) Petitioner had a follow up appointment for her fibromyalgia with Dr. Klein on September 27, 2019. (Ex. 90, pp. 34-37.) Petitioner reported that she underwent POTS testing. (*Id.* at 34.) Dr. Klein considered Ehlers Danlos syndrome[4] as a potential diagnosis for petitioner. (*Id.* at 37.) Later that year, on December 24, 2019, petitioner had another appointment with Dr. Klein for fibromyalgia. (Ex. 94, pp. 37-40.)

Petitioner had a follow up appointment with Dr. Vuppala on January 16, 2020. (Ex. 96, pp. 3-8.) Dr. Vuppala recounted petitioner's history, and then noted that her POTS screening "did not show any evidence of autonomic dysfunction." (*Id.* at 3-4.) Petitioner reported that her episodes continued. (*Id.* at 3.) On April 7, 2020, petitioner had a follow up appointment with Dr. Klein regarding her fibromyalgia. (Ex. 90, pp. 8-11.) Petitioner began seeing Michael Summers, M.D., a sleep medicine specialist, on May 13, 2020. (Ex. 96, pp. 14-18.) Dr. Summer's impression of petitioner included hypersomnolence, "out of proportion to what one would expect given the amount of sleep she gets," and seizure disorder. (*Id.* at 15.) Petitioner reported, again, that she had been healthy until 2015 when, 15 days after she received the MMR vaccine, she began to suffer from falls. (*Id.* at 16.) Petitioner reported that her symptoms improved when she was on seizure medication but not when she was on narcolepsy medication. (*Id.*) Dr. Summers explained that he wanted to confirm her diagnosis before progressing petitioner's treatment. (*Id.*) Finally, on December 1, 2020, petitioner was evaluated by Carey Ann Ronspies, M.D. for "features of a genetic disorder of connective tissue and common co-morbidities." (*Id.* at 19.) Dr. Ronspies also noted that petitioner has a history of recurrent falls, seizure disorder, narcolepsy and cataplexy, anxiety and depression, fibromyalgia, and hypokalemia. (*Id.*) Dr. Ronspies explained that petitioner's symptoms are not typical of hereditary Ehlers Danlos syndrome and recommended genetic testing to confirm a diagnosis given her complex history. (*Id.* at 19-20.)

[4] Ehlers Danlos Syndrome is defined as "a group of inherited disorders of connective tissue." *Ehlers-Danlos syndrome,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=110561 (last visited April 12, 2024). Symptoms include "hyperextensible skin and joints, easy bruisability, and friability of tissues with bleeding and poor wound healing." (*Id.*)

On March 3, 2021, petitioner had an appointment with Nurse Practitioner Kiley J. Meyer for lightheadedness. (Ex. 106, pp. 7-9.) Ms. Meyer explained that petitioner "may have POTS." (*Id.* at 7.) She noted that petitioner had not undergone testing to confirm this diagnosis, but she had increased her fluid and salt intake, mitigating her symptoms. (*Id.*) Petitioner's care for Ehlers Danlos syndrome, periodic paralysis, seizures, POTS, narcolepsy, and other conditions continued throughout 2022. (Ex. 105.)

b. As Reflected in Affidavits and Testimony

i. Petitioner's affidavits and testimony

Petitioner submitted two affidavits in this case, one on November 29, 2018 and the second on January 24, 2023, and testified at the entitlement hearing. (Exs. 2, 107; Tr. 4-50, 221-25.) Before her vaccination, petitioner reported that she was "an active person in [her] community." (Ex. 2, ¶ 3.) She "worked at [her] local YMCA in the toddler room as the staff lead . . . overs[eeing] 12-16 children age [two to four]," and as a waitress. (*Id.* ¶¶ 4, 8.) Additionally, she volunteered at the human society, Susan G. Komen for the Cute, Nebraska Children's Home, among other organizations, and "worked as a character actress for a party planning company. (*Id.* ¶¶ 5-7.) Petitioner also cared for her two dogs. (*Id.* ¶ 10.) She spent time sewing, reading, and organizing local comic book conventions. (*Id.* ¶¶ 12-14.)

Petitioner testified that she received a flu vaccine on October 15, 2015, and an MMR vaccine on October 21, 2015. (Ex. 2, ¶ 2; Tr. 11.) She explained that she did not experience an adverse reaction after her flu vaccine, however, about one week after receiving the MMR vaccine, she noticed that she "started to feel extremely tired, extremely fatigued, and irritable." (Tr. 12.) At first, she attributed this to being overworked and stressed. (*Id.*) She explained that her first memorable experience began when she attended a conference. (*Id.* at 12-13.) She explained that, after checking into her hotel room, she got dizzy while unpacking and vomited. (*Id.* at 13-14.) Over the next three days, she continued to feel awful and experience vertigo. (*Id.* at 14.) She described how pain "radiat[ed] down [her] neck and spine, out to . . . her fingers and hands." (*Id.*) Petitioner was unable to attend any of the conference. (*Id.* at 14-15.) She stated that she remembered feeling betrayed by her body. (*Id.*) She called her primary care physician and the on call nurse diagnosed her with the flu and instructed her to drink fluids and rest. (Ex. 2, ¶ 21.)

The day after petitioner got home from the conference, petitioner testified that she "stood up to go to the restroom and then [she] woke up on the floor having urinated [her]self." (Tr. 15-16; Ex. 2 ¶ 23.) She explained that she believes she experienced "a partial seizure of the memory loss and the fear." (Tr. 16.) She called her primary care physician again, and again was told she had the flu. (Ex. 2, ¶ 25.) Petitioner booked the next available appointment with her primary care physician. (Tr. 16.) She explained that going to the emergency room was cost prohibitive at the time. (*Id.*) Two days after that, on November 11, 2015, petitioner also began to experience pain in her hands,

wrists, hips, and ankles. (*Id.* at 18; Ex. 2, ¶ 26.) Petitioner explained that at that time she was also experiencing symptoms of cataplexy due to extreme stress. (Tr. 18-19.) Additionally, she described having night terrors and falling asleep during the day. (*Id.* at 19.)

Her symptoms became chronic overtime and she explained that she began to see specialist physicians in the hope of getting a better idea of what was going on with her. (Tr. 19-20.) Petitioner explained that she underwent an MSLT at a sleep clinic and was diagnosed with narcolepsy. (*Id.* at 21.) She has not received a study since because she would have to go off her medications and fears the impact on her life if she stopped taking her medications. (*Id.* at 21-22.) Petitioner was diagnosed with Complex Partial Seizures, which "cause [her] to enter a state of impaired consciousness or to lose consciousness altogether." (Ex. 2, ¶ 28.) Additionally, she has been diagnosed with POTS, which causes "dizziness, blurred vision, nausea and vomiting, brain fog, chest pain, blood pooling in [her] hands or feet, headaches, neck pain, insomnia, and shaking." (*Id.* ¶ 32.) Petitioner has also been diagnosed with fibromyalgia, causing "severe joint and muscle pain;" chronic fatigue syndrome, causing constant fatigue and mental fog; headaches; and numbness in her hands and feet. (*Id.* ¶ 36; Tr. 24-28.) Petitioner also suffers from migraines, but it is unknown whether this is a symptom of her other conditions. (Ex. 2, ¶ 38.) She explained that her current medications cause gastrointestinal issues, and she has trouble regulating her emotions. (*Id.* at ¶¶ 8-11; Tr. at 32-33.)

Petitioner testified that she was 22 years old when her symptoms began and that her life had changed significantly since her diagnoses. (Tr. 9.) She explained that, to have a good day, she cannot do anything physically exerting or stressful. (*Id.* at 9-10.) She sleeps for about 10 hours for her narcolepsy and has increased her water and sodium intake to keep her blood pressure in check. (*Id.* at 10.) She has to plan three to four days ahead to ensure her narcolepsy and her POTS are not triggered. (*Id.* at 10-11.) Petitioner testified that before she developed narcolepsy, she did experience some sleep issues, however, she explained that these were normally experiences and she felt like her narcolepsy symptoms were not normal. (*Id.* at 40-43.) Additionally, petitioner explained that she had always experienced some pain in her hands and wrists, however, the pain was different after she had been vaccinated. (*Id.* at 44.) After petitioner's diagnoses, she lost her job and was unable to volunteer, or work as a seamstress. (Ex. 2, ¶ 16.) Petitioner moved back in with her parents and has been unable to drive. (*Id.* ¶¶ 17, 19.) Her quality of life has been reduced greatly and she must use a wheelchair and avoid large gatherings altogether. (*Id.* ¶¶ 39-40.) Petitioner testified that she initially did not believe her condition was related to her vaccines. (Tr. 29.) However, after about six months, she read the labels on the vaccines and began to believe her vaccines had caused her conditions. (*Id.* at 29-30.)

Petitioner described how her condition has impacted her family, especially her grandparents, which has contributed to her feelings of anxiety, guilt, and depression. (Ex. 2, ¶¶ 12-13, 17.) Additionally, petitioner explained that her condition has led to increased financial strain on both her and her family. (*Id.* ¶¶ 13, 15-16.) She has a

service dog, however, "obtaining, training, and caring" for the dog has also created additional financial strain. (*Id.* ¶ 14.) Petitioner explained that her "injury has forever changed [her] on the inside and outside." (*Id.* ¶ 18.)

ii. Other witness statements

Petitioner has submitted eight witness statements in this case provided by family members and friends. (Exs. 9-16.) All of these affidavits explain that petitioner's condition has greatly impacted her life and that onset of her condition followed her vaccinations. (*Id.*) I have reviewed and considered all of these statements; however, none of the specific recollections contained in these statements effect the causal analysis below.

IV. Expert Opinions

a. Petitioner's Expert, Yuval Shafrir, M.D.[5]

Dr. Shafrir's opinion offers a very broad scope, discussing numerous conditions that he opines may help explain petitioner's overall clinical presentation. However, his theory of causation is comparatively narrow. Therefore, I have relied on extensive footnoting within this summary to address these many conditions while also maintaining focus on the operative aspects of Dr. Shafir's theory. However, the analysis that follows does, at points, incorporate these footnotes by reference.

All three of Dr. Shafrir's reports include an extensive discussion of petitioner's medical history interwoven with editorialization. (Ex. 25, pp. 1-41; Ex. 93; Ex. 98, pp. 3-17.) Ultimately, he concludes that there is "decisive evidence" that petitioner was in

[5] Dr. Shafrir provided three reports (Exs. 25, 93, and 98) and also testified during the entitlement hearing (Tr. 51-141, 212-224). During the hearing, he was proffered without objection as an expert in neurology and epileptology. (*Id.* at 56.) Petitioner additionally sought to present Dr. Shafrir as an expert in neuroimmune disorders, but respondent objected, arguing that Dr. Shafrir had not demonstrated any specialized experience with neuroimmune disorders beyond what would be seen by a practicing neurologist. (*Id.*) Upon later cross-examination, Dr. Shafrir confirmed that he had no training in immunology subsequent to medical school. (*Id.* at 105.) Dr. Shafrir received his medical degree from the Sackler School of Medicine at Tel Aviv University in 1982. (Ex. 26, p. 1.) Between 1983 and 1988, he completed a residency in pediatrics at Kaplan Hospital in Rehovot, Israel, Beilinson Medical Center in Petah Tikvah, Israel, and North Shore University Hospital in Manhasset, New York. (*Id.* at 1-2.) He then completed a pediatric neurology residency and fellowship at the Washington University Medical Center in St. Louis, Missouri. (*Id.* at 2.) In 1992, Dr. Shafrir completed his pediatric neurophysiology and epileptology fellowship at Miami Children's Hospital. (*Id.*) He is board certified in pediatrics as well as in neurology, with a special qualification in child neurology, and clinical neurophysiology. (*Id.*) Dr. Shafrir's clinical career has been dedicated to pediatric neurology. (*Id.* at 2-4.) Since 2019, Dr. Shafrir has conducted a private practice in which he sees about 10 patients a week and also works one to two weeks per month at various hospitals locum tenens. (Tr. 53.) He primarily sees patients with neuroimmune disorders, including PANDAS, PANS, chronic fatigue syndrome, and POTS. (*Id.*) Dr. Shafrir has co-authored several publications in various neurology journals, including publications addressing seizures and epilepsy, but not any relating to the other conditions at issue in this case. (Ex. 26, pp. 4-5.) Considering all of this, and the record as a whole, Dr. Shafrir is accepted for purposes of this decision as an expert in neurology and epileptology, but not neuroimmune disorders in particular.

good health and with normal function prior to vaccination and then experienced an abrupt and dramatic decline in function beginning about two weeks after vaccination. (Ex. 25, pp. 42-43.) Dr. Shafrir indicates that petitioner's multiple diagnoses are a "major problem" in analyzing petitioner's case. (*Id.* at 43.) He does not fault petitioner as "doctor shopping," but suggests that many of her doctors failed to address her presentation holistically. (*Id.*) He finds Dr. Joseph Shehan's assessment to have been the most reliable. (*Id*. at 43-44.) He is critical of the fact that several medical entries stress petitioner's "flu-like illness" at the time of onset without acknowledging her prior vaccinations. (*Id*.)

Dr. Shafrir opines that petitioner presented with a "progressive symptom complex" that included "identifiable components" of:

- Narcolepsy with possible cataplexy
- Presumed partial complex seizures
- Possible hypokalemic periodic paralysis
- Muscle spasms
- Generalized weakness, in particular weakness of upper extremities
- Fatigue
- Postural Orthostatic Tachycardia Syndrome (POTS)
- An onset of relatively severe psychiatric disorder with depression and incapacitating anxiety
- Nausea and vomiting
- Polyarthralgia
- Pain in her hands and also in the feet

(*Id*. at 44.) Given these features, he opines that petitioner's clinical picture "fit[s] very well" with the criteria for myalgic encephalomyelitis, otherwise known as chronic fatigue syndrome. (*Id*. at 44-45 (citing IOM (Institute of Medicine), *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome,* NAT. ACAD. PRESS 1 (2015) (Ex. 27)).) Dr. Shafrir explains that, though common, this condition is a syndrome "the etiology of which has not been yet clarified." (*Id*. at 45.) However, he opines that autoimmunity "is probably the most common biologic explanation." (*Id*. (citing Jonas Bloomberg et al., *Infection Elicited Autoimmunity and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: An Explanatory Model,* 9 FRONTIERS IMMUNOLOGY 1 (2018) (Ex. 28); Franziska Sotzny et al., *Myalgic Encephalomyelitis/Chronic Fatigue Syndrome – Evidence for an Autoimmune Disease,* 17 AUTOIMMUNITY REVS. 601 (2018) (Ex. 29))[6].)

[6] It is important to stress, as Dr. Shafrir acknowledges in his report, that these two papers do not establish that chronic fatigue syndrome is autoimmune, they merely hypothesize that it may be. For example, Blomberg, et al, specifically explain that "much work remains before the autoimmune nature of ME/CFS can be considered established" and further explain that evidence suggesting a metabolic etiology for the condition does not fit well into the proposed model. (Bloomberg et al., *supra,* at Ex. 28, p. 11.) During the hearing, Dr. Shafrir cited a finding from Sotzny, et al., that 20% of patients had symptom relief with Rituximab as "decisive proof" that chronic fatigue syndrome is autoimmune. (Tr. 89-91.) However, Sotzny, et al, indicate that, while there is "convincing evidence" of autoimmunity in at least a subset of chronic fatigue syndrome cases, the pathomechanism is incompletely understood and likely involves a combination of dysregulation within the immune, autonomic, and metabolic systems. (Sotzny et al., *supra,* at Ex. 29, pp. 1-2.) I am aware of one prior decision by a different special master finding a

He also notes that chronic fatigue can be a feature of patients with other rheumatologic and autoimmune conditions. (*Id*. (citing Mark R. Zielinski et al., *Fatigue, Sleep and Autoimmune and Related Disorders,* 10 FRONTIERS IMMUNOLOGY 1 (2019) (Ex. 30); Gerwyn Morris et al., *Central Pathways Causing Fatigue in Neuro-Inflammatory and Autoimmune Illnesses,* 13 BIOMED CENT. MED. 1 (2015) (Ex. 31).[7]) Dr. Shafrir cites a single paper hypothesizing that chronic fatigue syndrome and fibromyalgia can be vaccine caused. (*Id*. (citing Jacob N. Ablin & Dan Buskila, *Fibromyalgia, Chronic Fatigue, Functional Disorders, and Vaccination: Where Do We Stand?, in* VACCINES & AUTOIMMUNITY 331 (Yehuda Shoenfeld et al. ed., 2015) (Ex. 32).[8]) He further cites two

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petitioner entitled to compensation for chronic fatigue syndrome caused by the flu vaccine. *Bryan v. Sec'y of Health & Human Servs.*, No. 14-898V, 2020 WL 7089841 (Fed Cl. Spec. Mstr. Oct. 9, 2020). However, the *Bryan* case was decided on a very different record and, in particular, based on a theory that has not been presented in this case. On this record, Dr. Shafrir has not preponderantly established that chronic fatigue syndrome is autoimmune.

[7] These two papers observe that fatigue occurs commonly in patients with a number of different autoimmune conditions. The authors propose neuroimmune and metabolic pathways that could explain how fatigue could be a consequence of otherwise established autoimmune conditions. However, fatigue remains a non-specific finding. (Zielinski et al., *supra,* at Ex. 30, p. 1 (explaining that "[f]atigue is multi-faceted and broadly defined, which makes understanding the cause of its manifestations especially difficult in conditions with diverse pathology including autoimmune diseases."); Morris et al., *supra,* at Ex. 31, p. 14 (stating that "[w]hen viewed as a whole these observations also support the view that severe intractable fatigue results from processes which are not disease specific but involved in disease pathogenesis.")) Dr. Shafrir additionally cites the package insert for the Fluzone vaccine as reporting fatigue within its post-marketing experience. (Ex. 25, p. 46 (citing *Fluzone Prescribing Information* [hereinafter Fluzone Package Insert], Ex. 35).) Again, however, this reference to fatigue does nothing to dispel the notion of fatigue as a non-specific symptom. Moreover, post-marketing experience generally represents unverified passive surveillance, which is not typically considered persuasive. Specifically, the package insert explains that the disclosed adverse events were "spontaneously reported" and "[b]ecause these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure." (Fluzone Package Insert, *supra,* at Ex. 35, p. 10.) The fact that fatigue can be seen in autoimmune conditions does not add significant support to Dr. Shafrir's assertion that chronic fatigue syndrome is autoimmune.

[8] This paper relies in substantial part on the assertion that another fatiguing illness, Gulf War Syndrome, is a vaccine-caused entity as well as a broader concept known as Autoimmune Syndrome Induced by Adjuvants or "ASIA," which purports to link vaccines to autoimmunity broadly. (Ablin & Buskila, *supra,* at Ex. 32.) I have addressed both of these concepts in greater detail in prior decisions, including discussion of many of the same papers cited by Ablin and Buskila. As explained in those decisions, these materials do not provide meaningful evidence supporting vaccine causation. *Skinner-Smith v. Sec'y of Health & Human Servs*., No. 14-1212V, 2022 WL 4116896, at *31-35 (Fed. Cl. Spec. Mstr. Aug. 15, 2022) (finding that literature relating to Gulf War Syndrome did not support petitioner's theory that the Tdap vaccine can cause chronic fatigue syndrome); *J.F. v. Sec'y of Health & Human Servs*., No. 13-799V, 2022 WL 5434214, at *29-32, n. 34 (Fed. Cl. Spec. Mstr. Sept. 9, 2022) (explaining that "petitioner is unpersuasive in advancing ASIA as sound and reliable for any purpose and my conclusion is that ASIA fails as a concept fundamentally and in toto.") These prior decisions, and others subsequently discussed below, are not binding and do not dictate the outcome of this case. *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1358 (Fed. Cir. 2019). However, special masters are meant to apply their accumulated experience. *Hodges v. Sec'y of Health & Human Servs*., 9 F.3d 958, 961 (Fed. Cir. 1993) (explaining that "Congress assigned to a group of specialists, the Special Masters within the Court of Federal Claims, the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, judging the merits of the individuals claims.") Though these prior decisions provide more detailed discussion, I find the Ablin and Buskila paper unpersuasive on this record in any event. Even if Dr.

case reports of post flu vaccine chronic fatigue syndrome[9] and a study examining fatigue following rubella vaccination.[10] (*Id*. at 45-46.)

Despite identifying chronic fatigue syndrome as fitting "very well" with petitioner's clinical syndrome, he further opines that "[a] multisystemic autoimmune condition" may explain these very unusual associations" in petitioner's case. (Ex. 25, p. 46.) Therefore, his report cites several additional conditions, each of which he asserts is also an autoimmune condition, as including symptoms relevant to petitioner's history. (*Id*.) During the hearing, Dr. Shafrir ultimately opined that in addition to chronic fatigue

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Shafrir had been successful in demonstrating that chronic fatigue syndrome is autoimmune, he still would not have preponderantly established that it can be caused or triggered by vaccination. *Accord Skinner-Smith,* 2022 WL 4116896.

[9] The two case reports are presented in a single paper. (Sean P, J. Lynch et al., *Should Influenza Vaccination be Mandatory for Healthcare Workers?,* 347 BRIT. MED. J. 1 (2013) (Ex. 33).) The authors disclaim the assertion of any causal relationship, explaining that "[a] definite causal relationship between vaccination and chronic fatigue syndrome is not claimed here, all that has been established is a possible temporal relationship." (*Id.* at 4.) Case reports are not wholly without evidentiary value; however, as anecdotal reports, they are considered an especially weak form of evidence. *See, e.g. Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) ("single case reports of Disease X occurring after Factor Y . . . do not offer strong evidence that the *temporal* relationship is a *causal* one—the temporal relationship could be pure random chance"), *aff'd*, 125 Fed. Cl. 251 (2014); *but see Paluck ex rel. Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 475 (2012) (noting that "the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.") Dr. Shafrir has not preponderantly established that the flu vaccine in particular can cause chronic fatigue syndrome.

[10] (Michal Morag et al., *Psychological Variables as Predictors of Rubella Antibody Titers and Fatigue – A Prospective, Double Blind Study,* 33 J. PSYCHIATRIC RSCH 389 (1999) (Ex. 34).) Dr. Shafrir characterizes this study as one reporting post-vaccination chronic fatigue syndrome. (Ex. 25, p. 45-46.) However, this is not accurate. While fatigue-related symptoms were examined 10 weeks post-vaccination, the aim of the study was to assess whether personality and other psychologic variables can predict antibody titers and then, by extension, whether psychological variables can then be used to predict post-vaccination fatigue. (Morag et al., *supra,* at Ex. 34, p. 1.) The study examined a cohort of subjects previously vaccinated for rubella and a cohort that had not previously been vaccinated. (*Id.*) Subjects were provided a questionnaire both before and after vaccination and antibody titers were measured at the time of the second questionnaire. (*Id*. at 2-3.) Subjects provided subjective reports of fatigue-related symptoms based on questions relating to Post Viral Fatigue Syndrome as defined by the CDC, but were not diagnostically screened for chronic fatigue syndrome. (*Id*.) The authors suggest that their findings show that subjects deemed to have higher-self-esteem (which they relate to lower stress) saw a better immune response to vaccination whereas those deemed more neurotic (which they relate to depression) had a less effective immune response. (*Id*. at 5.) Regarding reports of fatigue, the authors posited that their results were consistent with factors of psychologic outlook as driving the subjects' degree of sensitivity to symptoms of fatigue. (*Id*. at 5-6.) The authors conclude that "[t]he findings of the present study underscore the importance of distinguishing between variables that influence general biases in symptom-complaining, and variables that help in predicting specific infection-induced effects." (*Id.* at 6.) Nothing in the study purports to establish that the rubella vaccine is a cause of chronic fatigue syndrome. Dr. Shafrir has not preponderantly established that the MMR vaccine can cause chronic fatigue syndrome.

syndrome petitioner should carry diagnoses of narcolepsy,[11] POTS,[12] epilepsy,[13] and, fibromyalgia.[14] (Tr. 58-59, 79.) He characterized depression and anxiety as "possible,"

[11] In his report and throughout much of his testimony, Dr. Shafrir did not distinguish between type one and type two narcolepsy (Ex. 25, p. 46), though some of his cited literature does. The distinction is important because respondent's expert, Dr. Evans, opines that only type one narcolepsy can be considered autoimmune. (Tr. 156-58.) During the hearing, Dr. Shafrir acknowledged that type one narcolepsy is associated with a particular HLA antigen (*see also* n. 21, *infra*), but asserted that the presence of that antigen is not a diagnostic requirement. (*Id.* at 68.) Thus, he testified that "by definition, [you] can have narcolepsy without this HLA." (*Id.* at 72.) But this testimony did not specifically resolve the distinction between type one and type two narcolepsy. It was not until he returned for rebuttal testimony that Dr. Shafrir specifically confirmed he is opining that petitioner suffered type one narcolepsy. (*Id.* at 214.) According to the literature Dr. Shafrir has provided, type one narcolepsy is characterized by either the presence of cataplexy and a positive multiple sleep latency test or hypocretin deficiency. (Sagarika Nallu & Selim R. Benbadis, *Narcolepsy,* MEDSCAPE (last updated Aug. 3, 2020) (Ex. 99, p. 3).) Dr. Shafrir has not preponderantly established that all forms of narcolepsy are autoimmune or that any type of narcolepsy beyond type one narcolepsy is autoimmune. The experts' disagreement as to whether petitioner suffered type one narcolepsy in particular turns on two issues, their disagreement as to the diagnostic significance of the HLA allele and their disagreement as to whether petitioner suffered cataplexy. As discussed under *Althen* prong two, below, I do not find it necessary to resolve the diagnostic question because I conclude that the HLA allele is critical to Dr. Shafrir's theory of causation regardless of whether it is diagnostic of type one narcolepsy.

[12] POTS is a condition affecting the autonomic nervous system resulting in tachycardia and orthostatic symptoms. Although Dr. Shafrir's opinion is premised on each of the conditions he has identified being autoimmune, he has acknowledged that POTS is a syndrome that has many causes. (Ex. 25, p. 47.) He includes two citations for the proposition that at least a subset of cases may be autoimmune. (*Id*. (citing Steven Vernino & Lauren E. Stiles, *Autoimmunity in Postural Orthostatic Tachycardia Syndrome: Current Understanding,* 215 AUTONOMIC NEUROSCIENCE: BASIC & CLINICAL 78 (2018) (Ex. 59); S. Dahan et al., *Postural Orthostatic Tachycardia Syndrome (POTS) – A Novel Member of the Autoimmune Family,* 25 LUPUS 339 (2016) (Ex. 60)).) I discussed extensively in a prior decision why there is not strong evidence supporting POTS as an autoimmune condition. *C.F. v. Sec'y of Health & Human Servs*., No. 15-731V, 2023 WL 2198809, at *31-36 (Fed. Cl. Spec. Mstr. Jan. 20, 2023). Even on a record that was far more developed on this issue than what has been presented in this case, I concluded that the petitioner had only demonstrated that it is "plausible, but yet to be established" that POTS has any autoimmune basis. *Id.* at 31. Based on my review of the Vernino and Stiles, and Dahen et al. papers cited in this case, their discussion of the autoimmune hypothesis of POTS is consistent with my discussion and conclusion in *C.F*. Dr. Shafrir has not preponderantly established on this record that POTS is either autoimmune or vaccine caused.

[13] Dr. Shafrir cites the following articles to support his assertion that epilepsy can be autoimmune: Mei-Sing Ong et al., *Population-Level Evidence for an Autoimmune Etiology of Epilepsy,* 71 J. AM. MED. ASS'N NEUROLOGY 569 (2014) (Ex. 64); Antonio Greco et al., *Autoimmune Epilepsy,* 15 AUTOIMMUNITY REVS. 221 (2016) (Ex. 65); M. Toledano et al., *Utility of an Immunotherapy Trial in Evaluating Patients with Presumed Autoimmune Epilepsy,* 82 NEUROLOGY 1578 (2014) (Ex. 66); Andrew McKeon, *Antibody Prevalence in Epilepsy (APE) Score—Evolution in Autoimmune Epilepsy Practice,* 74 J. AM. MED. ASS'N NEUROLOGY 384 (2017) (Ex. 67); James B. Lilleker et al., *VGKC Complex Antibodies in Epilepsy: Diagnostic Yield and Therapeutic Implications,* 22 SEIZURE 776 (2013) (Ex. 68); Eoin P. Flanagan et al., *Basal Ganglia T1 Hyperintensity in LGI1-Autoantibody Faciobrachial Dystonic Seizures,* 2 NEUROLOGY NEUROIMMUNOLOGY & NEUROINFLAMMATION 1 (2015) (Ex. 69); Claude Steriade et al., *Electroclinical Features of Seizures Associated with Autoimmune Encephalitis,* 60 SEIZURE: EUR. J. EPILEPSY 198 (2018) (Ex. 70). Dr. Evans indicates that autoimmune epilepsy occurs specifically within the context of autoimmune encephalitis, which he asserts has a distinct clinical presentation. (Ex. A, p. 13.) Upon my review, I do not see where any of the literature cited by Dr. Shafrir would necessarily contradict that explanation, though two of the papers do otherwise discuss epilepsy as being comorbid to several other

but "much more difficult to relate it to a particular autoimmune attack." (*Id.* at 58.) Although petitioner has also asserted that she had a preexisting migraine disorder that was significantly aggravated as part of her alleged vaccine injury (ECF No. 98, p. 10.), Dr. Shafrir indicated during the hearing that he did not believe petitioner's migraines were implicated as part of her alleged post-vaccination condition.[15] (Tr. 63.)

In summarizing his medical theory, Dr. Shafrir reiterates that the clinical picture fits chronic fatigue syndrome but concludes that given its other unusual features "I cannot think of any better unifying diagnosis beside an autoimmune process." (Ex. 25, p. 49.) Dr. Shafrir includes a number of citations for the general proposition that both the flu and MMR vaccines have been associated with autoimmune phenomenon

types of autoimmune disorders. (Ong et al., *supra,* at Ex. 64; Greco et al., *supra* at Ex. 65.) Dr. Shafrir has not opined that petitioner suffered an autoimmune encephalitis. (Tr. 94-95.) Dr. Shafrir has not preponderantly established on this record that any form of autoimmune epilepsy is implicated. In fact, he acknowledged during the hearing that he felt this was a less well established diagnosis for petitioner as compared to the other conditions he advanced. (*Id.*)

[14] Dr. Shafrir provides two citations to explain the etiology of fibromyalgia. (Ex. 25, p. 47 (citing Camillo Giacomelli et al., *The Interaction Between Autoimmune Diseases and Fibromyalgia: Risk, Disease Course and Management,* 9 EXPERT REV. CLINICAL IMMUNOLOGY 1069 (2013) (Ex. 61); Dan Buskila et al., *Etiology of Fibromyalgia: The Possible Role of Infection and Vaccination,* 8 AUTOIMMUNITY REVS. 41 (2008) (Ex. 62)).) They do not support the conclusion that it is either autoimmune or vaccine-caused. Giacomelli, et al, state that "Fibromyalgia (FM) is a common non-autoimmune rheumatologic disease with a wide range of symptoms that worsen the clinical status of patients. Several authors have tried to identify a putative autoimmune biomarker, but unfortunately, without positive results." (Giacomelli et al., *supra,* at Ex. 61, p. 1.) Buskila, et al., indicate that fibromyalgia is often seen in patients with autoimmune disease, and it may itself involve immunological aberration, but stop short of concluding it is itself autoimmune. (Buskila et al., *supra,* at Ex. 62, pp. 1-2.) They further explain that current evidence linking fibromyalgia to vaccination is only "anecdotal" and that any role for vaccination in precipitating fibromyalgia "still remains to be established." (*Id*. at 3.) Dr. Shafrir provided a third citation to a study by Klein, et al., for the proposition that chronic pain has been described as a manifestation of potassium channel autoimmunity, which he also otherwise implicates within his theory. (Ex. 25, p. 47 (citing Christopher J. Klein et al., *Chronic Pain as a Manifestation of Potassium Channel-Complex Autoimmunity,* 79 NEUROLOGY 1136 (2012) (Ex. 63)).) However, the Klein study was specifically accounted for by Giocomelli, et al., in their assessment of fibromyalgia etiology. (Giacomelli et al., *supra,* at Ex. 61, p. 3.) They concluded that the proposed antibodies have not been validated as a useful biomarker for fibromyalgia. (*Id*.) Thus, on this record Dr. Shafrir has not preponderantly established that fibromyalgia is either autoimmune or vaccine caused.

[15] In his report, Dr. Shafrir also referenced hypokalemic periodic paralysis and acquired neuromyotonia as additional conditions implicated by petitioner's medical records. (Ex. 25, p. 46.) However, he stopped short of asserting petitioner actually suffered these conditions. (*Id*.)

generally and that molecular mimicry,[16] epitope spreading,[17] and bystander activation[18] and have been proposed as potential explanations.[19] Ultimately, however, he indicates that "[o]ther than a few rare cases, the exact mechanisms by which infections or vaccinations can induce autoimmune disease has not been fully clarified." (*Id*.)

More specifically, Dr. Shafrir asserts that molecular mimicry has specifically been demonstrated in the context of narcolepsy caused by the flu vaccine.[20] (Ex. 25, p. 49.) This ultimately represents the crux of Dr. Shafrir's theory. However, he acknowledged that "even in the case of narcolepsy and influenza vaccination we are far from understanding the full mechanism. For example, only a tiny minority of the patients who carry the major risk factor of HLA DQB1*06:02/DQA1*01:02[21] and received the H1N1

[16] According to the literature cited by Dr. Shafrir, "molecular mimicry" occurs when "[c]ross-reactivity between a foreign antigen (such as a microorganism's peptides) and self antigens induces a break of self tolerance and leads to autoimmunity." (Nancy Agmon-Levin et al., *Vaccines and Autoimmunity,* 5 NATURE REVS. RHEUMATOLOGY 648, 650 (2009) (Ex. 84, p. 3 (Box 2)).)

[17] Dr. Shafrir's reference defines "epitope spreading" as "[b]roadening or diversification of the initial immune response from the dominant epitope to subdominant (cryptic) epitopes. Thus, the response to a single peptide spread to several responses directed at different epitopes either within the same antigen (intramolecular spreading) or in other antigens (intermolecular spreading)." (Agmon-Levin et al., *supra,* at Ex. 84, p. 3 (Box 2).)

[18] Dr. Shafrir's reference defines "bystander activation" as occurring when "[t]he initial immune response to an antigen might induce tissue damage and the release of sequestered antigens. These newly exposed antigens activate autoreactive lymphocytes (that is, T cells) that were not directly involved in the initial response. In addition, antigen-presenting cells activated by the initial antigen are capable of further activating macrophages, which perturb preprimed autoreactive T cells in a bystander manner." (Agmon-Levin et al., *supra,* at Ex. 84, p. 3 (Box 2).)

[19] In his report Dr. Shafrir also referenced polyclonal activation, but during the hearing indicated he does not believe that concept is implicated in this case. (Ex. 25, p. 49; Tr. 99.)

[20] The following articles pertaining to allegedly vaccine-caused narcolepsy have been filed in this case: Guo Luo et al., *Autoimmunity to Hypocretin and Molecular Mimicry to Flu in Type 1 Narcolepsy,* 115 PROC. NAT'L ACAD. SCI. E12323 (2018) (Ex. 37); Syed Sohail Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2,* 7 SCI. TRANSLATIONAL MED. 1 (2015) (Ex. 38); Markku Partinen et al., *Increased Incidence and Clinical Picture of Childhood Narcolepsy Following the 2009 H1N1 Pandemic Vaccination Campaign in Finland,* PUB. LIBR. SCI. ONE e33723 (2012) (Ex. 39) (also filed as Ex. A, Tab 14); Richard E. Rosch et al., *Narcolepsy Following Yellow Fever Vaccination: A Case Report,* 7 FRONTIERS NEUROLOGY 1 (2016) (Ex. 40); Sebjorg Elizabeth Hesla Nordstrand et al., *Psychiatric Symptoms in Patients with Post-H1N1 Narcolepsy Type 1 in Norway,* 42 J. SLEEP 1 (2019) (Ex. 41); Anna-Helena Saariaho et al., *Autoantibodies Against Ganglioside GM3 are Associated with Narcolepsy-Cataplexy Developing After Pandemrix Vaccination Against 2009 Pandemic H1N1 Type Influenza Virus,* 63 J. AUTOIMMUNITY 68 (2015) (Ex. 42); Segal & Shoenfeld, *supra,* at Ex. 85.

[21] "HLA" refers to "human leukocyte antigens," which are histocompatibility antigens governed by genes of the HLA complex, a chromosome region containing multiple alleles – *i.e*. genetic variants at different loci. *Human leukocyte antigens*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=56923 (last visited April 12, 2024). The letters "DQ" identify the location of the allele at issue and "B1" and "A1" identify the specific allele. *Id*. The alleles are in turn associated with antigens that are typed by their serologic reactions. *Id*. DQB1*0602 is a class II HLA molecule that "initiate[s] the adaptive immune response by presenting short, pathogen-derived peptides to T cells." If a self-peptide is presented, this can lead to autoimmune disease. (*See* Nathaniel

vaccine with the offensive adjuvant actually developed narcolepsy." (*Id*. at 49-50.) Thus, he opines that petitioner's influenza vaccine "produced an initial autoimmune response against multiple components of multiple systems in her body" and "[a] reasonable candidate is an initial process that produces antibodies against components of the potassium channel and against the hypocretin receptor" as seen in narcolepsy. (*Id*. at 50.)

During the hearing, Dr. Shafrir further explained his theory as follows: "[W]e have several conditions that are presumably autoimmune and I explain why, and then in one of them we have a good explanation so I make the assumption that it's the same process in the other, where the mechanism is not known." (Tr. 107-08.) Specifically, he testified that:

> [O]ne of the conditions she has is narcolepsy, and in contrast to most other vaccine-related injury, in narcolepsy we have some, not full in any way, but some understanding of the mechanism. So we know that in narcolepsy they demonstrated actually molecular mimicry as the mechanism, and the production of antibodies affecting both – in this particular case, the influenza vaccine, and the hypocretin receptor and the hypocretin molecule itself.

(*Id.* at 97.) He asserts that epitope spreading and bystander activation can explain how the autoimmune reaction leading to narcolepsy can lead to further attack on other targets that were not attacked in the initial autoimmune reaction. (*Id.* at 98; Ex. 25, p. 50 (citing Agmon-Levin et al., *supra,* at Ex. 84); Yahel Segal & Yehuda Shoenfeld, *Vaccine-Induced Autoimmunity: The Role of Molecular Mimicry and Immune Crossreaction,* 15 CELLULAR & MOLECULAR IMMUNOLOGY 586 (2018) (Ex. 85)).)

Dr. Shafrir asserts that all of the conditions he identified as present in petitioner's case arose simultaneously on November 6, 2015, at the time of the abrupt illness she described in her testimony. (Tr. 135-36.) He opines that this timing is appropriate to infer vaccine-causation. (*Id.* at 99-100.)

F. Watson et al., *Does Narcolepsy Symptom Severity Vary According to HLA-DQB1*0602 Allele Status?,* 33 Sleep 29 (2010) (Ex. 101); *see also* Rama J. Wahab et al., *Celiac Disease Autoimmunity and Emotional and Behavioral Problems in Childhood,* 144 Pediatrics 1 (2019) (Ex. 73); Takashi Kanbayashi et al., *Symptomatic Narcolepsy in Patients with Neuromyelitis Opticia and Multiple Sclerosis,* 66 Archives Neurology 1563 (2009) (Ex. 46); *but see* M. Vitiello et al., *Type on Narcolepsy in Anti-Hu Antibodies Mediated Encephalitis: A Case Report,* 47 Congresso Nazionale 1 (2017) (Ex. 44) (narcolepsy patients negative for HLA DQB1*0602 alleles).) In particular, "[h]igher levels of surface expression of HLA DQB1*0602 on antigen-presenting cells […] could increase the likelihood that hypocretin producing cell autoantigens" are presented to T cells. (Watson et al., *supra,* at Ex. 101, p. 5.) Thus, DQB1*0602 has been specifically implicated as having "direct involvement" in susceptibility to narcolepsy. (*Id*. at 1.) References to "DQB1*0602" can relate to either allele status or the resulting histocompatibility antigen.

b. Respondent's Expert, M. Steven Evans, M.D.[22]

Dr. Evans agrees that petitioner had a complicated medical history without any definitive diagnosis. (Ex. A, p. 7.) He particularly stressed Dr. Shehan's summary that petitioner's "litany of different issues" represented "one of the most complicated patients I take care of" with increasing spells that are "very unusual." (*Id*. (quoting Ex. 90, p. 107).) Dr. Evans notes that many diagnoses were considered despite only having weak support and that many of her diagnoses are for very different types of conditions that typically do not co-occur. (*Id*.) Because petitioner suffered episodes of sudden loss or alteration of consciousness, he finds it reasonable that narcolepsy and epilepsy were the two most prominently considered conditions. (*Id*. at 8.) However, he opines there is ultimately inadequate evidence to support either diagnosis. (*Id.* at 7-10.) Based on his review of the subsequently filed medical records, Dr. Evans confirmed in a second report that his opinion did not change. (Ex. C, p. 5.) Dr. Evans provided extensive discussion of the diagnostic considerations at issue; however, in light of the analysis that follows, it is not necessary to detail the points he raised.

Dr. Evans acknowledges that there are some pieces of literature, largely case reports, hypothesizing that conditions such as chronic fatigue syndrome, POTS, and fibromyalgia, are autoimmune; however, he characterizes that evidence as very weak and does not agree that any of the conditions are autoimmune. (Tr. 205-07.) Regarding narcolepsy, Dr. Evans explains that only type one narcolepsy is thought to be autoimmune. (*Id.* at 156-58.) Whereas type two narcolepsy involves the loss of orexin-containing neurons, type one narcolepsy involves the loss of hypocretin neurons. (*Id*.) Type one narcolepsy is associated with a specific allele (HLA-DQB1*06:02). (*Id.*; Ex. A, p. 8.) However, Dr. Evans does not agree that the flu vaccine (even including the Pandemrix vaccine) has been established via molecular mimicry as a cause of type one narcolepsy. (Tr. 176.)

In this case, Dr. Evans notes that petitioner was specifically tested for the HLA-DQB1*06:02 allele and the test was negative; therefore, he opines that this finding weighs "strongly" against any diagnosis of narcolepsy at all, leaving the diagnosis "speculative" in petitioner's case. (Ex. A, p. 8.) However, to the extent it does not

[22] Dr. Evans submitted two reports and also testified at the hearing. (Exs. A, C; Tr. 141-210.) He was proffered without objection as an expert in neurology and epileptology. (Tr. 144.) He graduated with his bachelors' degree from the University of Kentucky and his medical degree and a Masters in Physiology from the University of Louisville School of Medicine. (Ex. B, p. 1.) He completed an internship, his residency in neurology, and a postdoctoral fellowship in neuropharmacology at Barnes Hospital/Washington University School of Medicine. (*Id.*) He is board certified by the American Board of Psychiatry and Neurology in clinical neurophysiology and epilepsy and by the National Board of Medical Examiners. (*Id.* at 4.) He currently works as a professor in the Department of Neurology at the University of Louisville and sees patients as the University of Louisville Hospital, Jewish Hospital in Louisville Kentucky, and Owensboro Health Regional Hospital. (*Id.* at 1-2.) At the time he submitted his CV to the court, he had written five book chapters and reviews, 42 peer-reviewed articles, and 72 abstracts. (*Id.* at 8-15.) Dr. Evan's inpatient practice included general neurology practice and a stroke program, and his outpatient practice focused primarily on epilepsy. (Tr. 143.) Dr. Evans also has a background in electroencephalopathy. (*Id.* at 144.)

definitively rule out any type of narcolepsy, it would be far more likely that petitioner would have type two narcolepsy. (Tr. 156-58.) Although this allele can be found in people who do not have narcolepsy, it is found in 98% of patients with type one narcolepsy.[23] (*Id*.; *see also* Hanna M. Ollila et al., *HLA-DPB1 and HLA Class I Confer Risk of and Protection from Narcolepsy,* 96 AM. J. HUM. GENETICS 136, 136 (2015) (Ex. A, Tab 13, p. 1).)

V. Discussion

Petitioner obviously has a complicated medical history and, as Dr. Shafrir explained, her medical history reflects a prolonged, and no doubt frustrating, search for a satisfactory explanation for her condition. That diagnostic uncertainty continues to be reflected in the competing expert opinions in this case. Dr. Shafrir opines that petitioner suffered simultaneous onset of the following conditions: narcolepsy, epilepsy, chronic fatigue syndrome, fibromyalgia, and POTS. (Ex. 25, p. 44.) Further, Dr. Shafrir opines that each of these conditions is autoimmune and that they can therefore be viewed collectively as a unified syndrome of autoimmunity. (*Id.* at 46, 49.) Dr. Evans largely disagrees on respondent's behalf. (Tr. 205-07, 156-58.) However, the purpose of this decision is not to resolve petitioner's search for a medical explanation. Instead, the purpose of this decision is to determine whether petitioner has met her own burden of proof with respect to whether her condition, either in whole or in part, was caused by the vaccine(s) at issue. *Accord Orgel-Olsen v. Sec'y of Health & Human Servs.*, 15-285V, 2022 WL 1598143, at *36 (Fed. Cl. Spec. Mstr. Mar. 11, 2022) (explaining in conclusion that "[p]erhaps unsurprisingly, however, this legal Program cannot achieve for petitioner the clarify that eluded his many treating physicians.")

Based on the theory petitioner has presented, it is not ultimately necessary to definitively catalog and categorize her symptoms. Dr. Shafrir is very clear in presenting petitioner's alleged narcolepsy as the linchpin of his theory of causation. Specifically, he opines that, of all the conditions he has discussed, he can locate good evidence only for his contention that narcolepsy can be caused by the flu vaccination. (Ex. 25, pp. 49-50; Tr. 97.) He opines only by extension from that condition that it is reasonable to conclude that the entirety of petitioner's presentation was also vaccine-caused. (Tr. 107-08.) Thus, regardless of whether petitioner would qualify for any of the other diagnoses, my conclusion that Dr. Shafrir has not preponderantly supported any vaccine-caused narcolepsy is dispositive. Therefore, the *Althen* analysis below focuses primarily on petitioner's alleged narcolepsy.

a. *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," demonstrating that the vaccine received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.,* 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting

[23] Dr. Shafrir disagrees with specifically placing the prevalence at 98%. (Tr. 71-72.) While he acknowledges this figure is included in some of the literature, he indicates that other literature has identified lower percentages. (*Id.*)

Pafford v. Sec'y of Health & Human Servs., No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004)). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen,* 35 F.3d at 548-49. Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.,* 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [her] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon,* 941 F.3d at 1359 (quoting *Knudsen*, 35 F.3d at 548-49).

Apart from narcolepsy, Dr. Shafrir has provided little to no direct evidence supporting the opinion that any of the conditions allegedly at issue can be caused by either of the vaccines at issue. Moreover, absent his reliance on autoimmune narcolepsy (*see* n. 11, 21, *supra*), Dr. Shafrir has not otherwise offered any other clearly articulated theory that would point to either vaccine as a cause of petitioner's condition. In particular, the evidence of record is insufficient to preponderantly establish a stand-alone causal theory for chronic fatigue syndrome, POTS, epilepsy, fibromyalgia, hypokalemic periodic paralysis or acquired neuromyotonia, or migraines. (*See* n. 6-10 (CFS), n. 12 (POTS), n. 13 (epilepsy), n. 14 (fibromyalgia), n. 15 (hypokalemic periodic paralysis/acquired neuromytonia) *supra*; Tr. 63.)

Instead, Dr. Shafrir premises his theory on the idea that there is sufficient evidence from which to conclude that the flu and/or MMR vaccines can cause type one narcolepsy via molecular mimicry. (Ex. 25, pp. 49-50; Tr. 97.) From that starting premise, he further opines that the specific concepts of epitope spreading and bystander activation permit the conclusion that the cause of one autoimmune condition can also be the cause of additional autoimmune conditions affecting other body systems. (Ex. 25, p.50; Tr. 98.) He therefore concludes that, because appropriate medical thinking seeks a unifying diagnosis, if one of petitioner's conditions is implicated as a vaccine-caused autoimmune condition, *i.e*. narcolepsy, then it is reasonable to also assume that her entire constellation of syndromes is likewise due to the same underlying cause. (Ex. 25, p. 46.) Upon my review of the record as a whole, none of these premises is well supported and Dr. Shafrir's theory is not sound and reliable.

The fact that type one narcolepsy is autoimmune does not automatically mean that any vaccine can cause the condition via molecular mimicry. Molecular mimicry is a hypothesis whereby a specific foreign antigen may have sufficient similarity to bodily tissue that the immune system is triggered to "cross-react" against the bodily tissue, *i.e*. to attack the body itself when activated to clear the foreign antigen. (*See* Segal & Shoenfeld, *supra,* at Ex. 85, p. 1.) Molecular mimicry "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 18,

2019)). During the hearing, Dr. Shafrir agreed, noting that "[i]t's not enough that you say that you think it's molecular mimicry," and explaining that asserting causation via molecular mimicry requires demonstration that mimicry between portions of the vaccine and components of the bodily tissue actually exists.[24] (Tr. 130-31.)

Incidences of type one narcolepsy have been shown to have increased following the H1N1 pandemic. (Fang Han et al., *Narcolepsy Onset is Seasonal and Increased Following the 2009 H1N1 Pandemic in China,* 70 ANNALS NEUROLOGY 410 (2011) (Ex. A, Tab 8).) Further, the record evidence includes several studies associating type one narcolepsy to a specific formulation of H1N1 pandemic strain flu vaccination called Pandemrix. (Partinen et al., *supra,* at Ex. 39; Nordstrand et al., *supra,* at Ex. 41; Saariaho et al., *supra,* at Ex. 42.) Additionally, Dr. Shafrir cited a study by Luo, et al., that proposed molecular mimicry between hemagglutinin within the Pandemrix vaccine and hypocretin peptides. (Luo et al., *supra,* at Ex. 37.) On cross-examination, however, he acknowledged that this study fell short of proving causality with respect to the autoantibodies it identified. (Tr. 108-09). A later study by Vuorela, et al., filed by respondent, also showed a pathogenic, cross-reactive role for influenza virus-specific T cells from the Pandemrix vaccine in causing type one narcolepsy. (A. Vuorela et al., *Enhanced Influenza A H1N1 T Cell Epitope Recognition and Cross-Reactivity to Protein-O-Mannosyltransferase 1 in Pandemrix-Associated Narcolepsy Type 1,* 12 NATURE COMMC'N 1 (2021) (Ex. C, Tab 6).) However, Vuorela, et al., implicated a different autoantigen (protein-O-mannosyltransferase 1) for the first time. The Vuorela authors otherwise noted Luo, et al, cited by Dr. Shafrir, to be among a body of conflicting literature regarding the cross-reactive potential of certain hypocretin epitopes. (Vuorela et al., *supra,* at Ex. C, Tab 6, p. 9.) Thus, even despite submitting the Vuorela, et al., study, Dr. Evans opines that the available evidence falls short of demonstrating molecular mimicry as a cause of Pandemrix-related type one narcolepsy, especially because an autoantigen has not been clearly identified. (Tr. 176.)

But in any event, safety reviews examining a number of different H1N1 pandemic flu vaccines confirmed that the elevated risk of narcolepsy was specific to the Pandemrix formulation. (Tomi O. Sarkanen et al., *Incidence of Narcolepsy After H1N1 Influenza and Vaccinations: Systematic Review and Meta-Analysis,* 38 SLEEP MED. REVS. 177 (2018) (Ex. A, Tab 16); Claudia Maria Trombetta et al., *Influenza Vaccines:*

[24] In point of fact, prior caselaw in this program persuasively establishes that identifying a mimic (*i.e.* homology) alone is not sufficient to meet a petitioner's burden of proof. Specifically, "the finding of sequence homology does not necessarily mean the similarity has significance to the immune system." *Tullio v. Sec'y of Health & Human Servs.*, No. 15-51V, 2019 WL 7580149, at *15 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), *aff'd,* 149 Fed. Cl. 448 (2020); *see also Caredio ex re. D.C. v. Sec'y of Health & Human Servs.,* No. 17-0079V, 2021 WL 4100294, at *31 (Fed. Cl. Spec. Mstr. July 30, 2021) ("*demonstration of homology alone is not enough to establish a preponderant causation theory*") (emphasis in original) (citing *Schultz v. Sec'y of Health & Human Servs.,* No. 16-539V, 2020 WL 1039161, at *22 n. 24 (Fed. Cl. Spec. Mstr. Jan. 24, 2020), *mot. for rev. denied,* 2021 WL 6058835 (Fed. Cl. Dec. 3, 2021). Nonetheless, petitioners in this program are not required to prove their theories to the level of scientific certainty. Prior cases have expressed with regard to the application of molecular mimicry that "[t]he line must be drawn somewhere between speculation and certainty." *Brayboy v. Sec'y of Health & Human Servs.,* No. 15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021).

Evaluation of the Safety Profile, 14 HUM. VACCINES & IMMUNOTHERAPEUTICS 657 (2018) (Ex. A, Tab 19).) One possible explanation for this is that the Pandemrix vaccine was unique with respect to the adjuvant it used. (*See* Partinen et al., *supra,* at Ex. 39, p. 7-8.) In that regard, the material Dr. Shafrir relies upon regarding molecular mimicry stresses the possible role of adjuvants in explaining autoimmunity. (Agmon-Levin et al., *supra,* at Ex. 84.) Thus, Dr. Shafrir does specifically opine that only the minority of vaccinees who received "the offensive adjuvant" actually developed narcolepsy. (Ex. 24, pp. 49-50.) Dr. Sharir also suggested that the Pandemrix vaccine may have had a higher dose of antigen as compared to other pandemic vaccines. (Tr. 114.)

In light of all this, there is no basis on this record for suggesting that the evidence pertaining to Pandemrix-caused narcolepsy is in any way generalizable to other vaccines, even other formulations of the flu vaccine. Petitioner's own expert opines that the causal relationship at issue is likely due to the specific formulation of the Pandemrix vaccine, which is not the vaccine petitioner received. (Ex. 25, pp. 49-50.) Nor, based on the expert testimony available in this case, is it even necessarily clear that the above-discussed literature establishes that molecular mimicry is the actual explanation for Pandemrix-caused narcolepsy. While both Vuorela, et al., and Luo, et al., provide some evidence supporting a molecular mimicry theory, the two studies are in tension in that each study identifies a different pathway. Ultimately, neither expert suggests the mechanism of causation is understood. (Vuorela et al., *supra,* at Ex. C, Tab 6; Luo et al., *supra,* at Ex. 37; Ex. 25, p. 49; Tr. 176.) In fact, while petitioner is not obligated to prove a mechanism, it is worth nothing that Dr. Shafrir's own characterization is that we are "far" from understanding the full mechanism of Pandemrix-caused narcolepsy. (Ex. 25, p. 49.) And, in any event, both the Vuorela and Luo studies were specific to the Pandemrix formulation of the H1N1 vaccine. (Vuorela et al., *supra,* at Ex. C, Tab 6; Luo et al., *supra,* at Ex. 37.)

Accordingly, for all these reasons, Dr. Shafrir has not presented a sound and reliable opinion theorizing that either the seasonal flu or MMR vaccines (as opposed to the Pandemrix vaccine) can cause narcolepsy.[25] This is a threshold issue that is fatal to Dr. Shafrir's theory, because he very clearly acknowledges that of all the conditions he has discussed, narcolepsy has the strongest supporting evidence and that it is only or

[25] Several prior decisions have similarly held that petitioners failed to preponderantly establish a theory of causation implicating the seasonal flu vaccine as a cause of narcolepsy. *D'Tiole v. Sec'y of Health & Human Servs.*, No. 15-85V, 2016 WL 7664475 (Fed Cl. Spec. Mstr. Nov. 28, 2016), *mot. rev. den'd*, 132 Fed Cl. 421 (2017), *aff'd* 726 Fed.Appx. 809 (Fed. Cir. 2018); *McCollum v. Sec'y of Health & Human Servs.*, No. 14-790V, 2017 WL 5386613 (Fed Cl. Spec. Mstr. Sept. 15, 2017), *mot. rev. den'd* 135 Fed. Cl. 735, *aff'd* 760 Fed.Appx. 1003 (Fed. Cir. 2019); *Dougherty v. Sec'y of Health & Human Servs.*, No. 15-1333V, 2018 WL 3989519 (Fed. Cl. Spec. Mstr. July 5, 2018), *mot. rev. den'd* 141 Fed. Cl. 223 (2018); *but see Henkel ex rel. V.H. v. Sec'y of Health & Human Servs.*, No. 15-1048V, 2022 WL 16557979 (Fed. Cl. Spec. Mstr. Aug. 31, 2022), *mot. rev. den'd* 165 Fed. Cl. 153 (2023). In the one prior case in which a petitioner did preponderantly establish a theory of causation linking the flu vaccine to narcolepsy, the petitioner's expert provided a substantially more detailed showing of molecular mimicry than what is available on this record, including specific demonstration of a proposed homology. *Henkel*, 2022 WL 16557979, at *35-43. Dr. Shafrir's theory in this case, while involving the same basic assertion, is not supported to anything close to the same degree.

primarily his ability to identify vaccine-caused narcolepsy that permits him to theorize that the remainder of petitioner's alleged conditions were also vaccine-caused. (Tr. 58-59, 97-99.)

Even assuming *arguendo* that Dr. Shafrir had been persuasive in contending that the vaccine(s) at issue can cause narcolepsy, his second premise – that epitope spreading and bystander activation can explain how one autoimmune process can cause all of the other autoimmune conditions alleged – is likewise entirely unsupported on this record. As with molecular mimicry, there is no debate that these are valid scientific principles in the abstract. Dr. Evans agrees that it is "possible but not proven" that these concepts could explain the presence of the multiple autoimmune conditions allegedly at issue. (Tr. 176.) However, Dr. Shafrir has not presented any support for the notion that either bystander activation or epitope spreading have been shown to be possible causes of any of the specific conditions at issue in this case, either alone or in combination.[26] Moreover, the specific papers Dr. Shafrir cites when invoking bystander activation and epitope spreading do not assert, let alone substantiate, that these concepts would work synergistically to cause a constellation of otherwise distinct autoimmune conditions in the manner Dr. Shafrir proposes. (Ex. 25, p. 50 (citing Agmon-Levin et al., *supra,* at Ex. 84; Segal & Shoenfeld, *supra,* at Ex. 85).) Rather, these papers reflect discussion of these mechanisms as various possible mechanisms that may or may not separately explain individual autoimmune conditions. (Agmon-Levin et al., *supra,* at Ex. 84; Segal & Shoenfeld, *supra,* at Ex. 85.) On the whole, they reflect that autoimmune conditions are influenced by many factors that are not well understood. The fact that a person may be prone to autoimmunity or experience multiple autoimmune conditions does not automatically lead to the conclusion that the one autoimmune condition is causally related the other(s).

In that regard, Dr. Shafrir's third premise reveals the speculative nature of his theory overall. In effect, Dr. Shafrir opines that the presence of one autoimmune condition in itself simply raises a suspicion that the same autoimmune process also explains any other condition or symptoms petitioner may have. (Ex. 25, p. 46.) Dr. Shafrir suggests that autoimmune diseases can be widespread, have broad diagnostic criteria, and "we have absolutely no idea why certain autoimmune diseases affect one place and not another place." (Tr. 61.) Thus, Dr. Shafrir testified that

> this is practically a basis tenet in medical thinking, medical reasoning, that you try to explain an entire syndrome with a unified diagnosis. So looking at this unified diagnosis, and knowing that at least one of her diagnoses, narcolepsy, is an autoimmune disease, and . . . we do not have any other explanation for this, you have to assume that autoimmune process was a cause of her other – the other component of her syndrome.

[26] By way of counter example, although the above-discussed Pandemrix vaccine has been shown to cause narcolepsy, Dr. Harris cited a largescale epidemiologic study that nonetheless found no increased risk of epileptic seizures following that vaccine. (Lisen Arnheim Dahlstrom et al., *Risk of Presentation to Hospital with Epileptic Seizures After Vaccination with Monovalent AS03 Adjuvanted Pandemic A/H1N1 2009 Influenza Vaccine (Pandemrix): Self Controlled Case Series Study,* 345 BRIT. MED. J. 1 (2012) (Ex. A, Tab 1).)

(Tr. 59.)

Dr. Shafrir's opinion on this point is self-contradictory. Dr. Shafrir's reasoning is based on the idea that a unifying diagnosis is preferred; however, he is clear in opining that petitioner does not have any unifying diagnosis that he can identify. Instead, he explicitly invokes several distinct diagnoses to explain her clinical presentation.[27] As discussed separately above, for most of the conditions at issue there is not preponderant evidence that they are autoimmune and the reasons for *suspecting* an autoimmune process are different in each instance. (*See* n. 6-10 (chronic fatigue syndrome), n. 12 (POTS, n. 13 (epilepsy), and n. 14 (fibromyalgia), *supra*.) Once Dr. Shafrir resorts to invoking multiple diagnoses to explain the overall clinical presentation, he has provided no scientific or medical explanation that would justify setting aside the finer etiologic understanding of each separate condition in favor of a unified syndrome for which no diagnosis exists. During the hearing, Dr. Shafrir acknowledged he is effectively proposing a novel syndrome that has never been described in literature or even identified by a single case report as vaccine caused. (Tr. 133-34.) To the extent Dr. Shafrir suggested that chronic fatigue syndrome could be a likely, if incomplete, unifying diagnosis, he has not preponderantly established that it is in itself an autoimmune condition or, even if it were, that it can be caused by vaccination. (*See* n. 6-10, *supra*.) When none of the conditions singularly have any strong suspicion of vaccine-causation there is no basis for then contending that they should somehow in combination support a different or stronger conclusion.

Dr. Shafrir's explicit testimony is that he is merely "assum[ing]" that if one identified condition has a known mechanism, then that mechanism must also explain petitioner's entire picture of health. (Tr. 58-59.) On cross-examination, he specifically testified that "we have several conditions that are presumably autoimmune and I explain why, and then in one of them we have a good explanation so I make the assumption that it's the same process in the other, where the mechanism is not known." (Tr. 107-08.) Even accounting for the fact that petitioner is not obligated to specifically prove an underlying mechanism, this is clearly speculative. Dr. Shafrir is seeking to leverage the shortcomings of our understanding of these conditions as affirmative evidence of a single underlying cause. However, this is simply not credible. The limits of our understanding of these conditions are the limits of our understanding, not evidence supporting some other hypothesis. As Dr. Shafrir himself puts it, "*we have absolutely no idea why* certain autoimmune diseases affect one place and not another place." (Tr. 61 (emphasis added).) The fact that petitioner's clinical presentation otherwise remains

[27] Petitioner explicitly confirmed this understanding in her prehearing reply brief. Respondent had argued that Dr. Shafrir's failure to identify a diagnosed beyond an "autoimmune process" broadly meant that no *Althen* analysis was necessary in this case due to the lack of an identified injury. (ECF No. 99, pp. 23-25 (citing Ex. 25, p. 49).) In reply, petitioner argued that "both Dr. Shafrir and Petitioner's treating doctors have in fact provided Petitioner with clear *diagnoses*." (ECF No. 101, p., 3 (emphasis added).) Note the plural. Petitioner continued, "Dr. Shafrir's statement regarding an 'autoimmune process' was not meant to be the be-all end-all diagnosis in his opinion, but rather just a statement made in trying to create a 'unifying' or umbrella term to demonstrate his opinion that all of Petitioner's issues were derived from the vaccination events." (*Id.*)

enigmatic does not mean that Dr. Shafrir's proffered explanation is either sound or reliable. Nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder ex. rel Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013).

For all these reasons, Dr. Shafrir fails to preponderantly establish not only that the vaccines at issue can cause narcolepsy, but also that autoimmune narcolepsy, if present, can in itself help to explain petitioner's broader constellation of symptoms. Accordingly, petitioner has not met her burden of proof under *Althen* prong one. And, importantly, this analysis stands regardless of whether Dr. Shafrir can separately establish that petitioner actually suffers any of the specific conditions he asserts.

b. *Althen* prong two

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326-27; *Grant*, 956 F.2d at 1147-48. Medical records are generally viewed as particularly trustworthy evidence. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. *See* § 300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder,* 88 Fed. Cl. at 746 n. 67 ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted.") A petitioner may support a cause-in-fact claim through either medical records or expert medical opinion. § 300aa-13(a). The special master is required to consider all the relevant evidence of record, draw plausible inferences and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.,* 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines,* 940 F.2d at 1528).

As discussed under *Althen* prong one, the crux of petitioner's theory is that she can demonstrate her entire clinical presentation to be vaccine-caused because, among her various conditions, she suffers autoimmune narcolepsy for which the Pandemrix flu vaccine has been implicated as a cause. However, even without resolving the experts' differences regarding whether petitioner can actually be diagnosed with type one narcolepsy specifically, petitioner's negative test for the DQB1*0602 allele is highly relevant and virtually fatal in itself to petitioner's claim.

Dr. Evans cited literature supporting the idea that the DQB1*0602 allele is present in an overwhelming proportion of type one narcolepsy patients, about 98%. (Ex. A, p. 8; Tr. 156-58; Ollila et al., *supra,* at Ex. A, Tab 13.) Dr. Shafrir acknowledged

that some literature does reflect the 98% prevalence of the HLA cited by Dr. Evans, but suggested the specific figure varies in different studies. (Tr. 71.) This is largely due to the strictness with which cataplexy may be defined among different studies. (Watson et al., *supra,* at 101, p. 5.) Thus, Dr. Shafrir countered that the allele is not necessary for diagnosis. (Tr. 70-72.) For example, he discussed a study by Watson, et al., that found that 58 out of 158 narcolepsy subjects did not have the particular HLA. (*Id.* at 71 (discussing Watson et al., *supra,* at 101).) Conversely, as Dr. Evans acknowledged, not everyone who has the allele suffers type one narcolepsy even as it remains highly prevalent among type one narcoleptics. (*Id.* at 156-58.)

Importantly, however, the Watson, et al., study cited by Dr. Shafrir concluded that there is a dose response relationship between allele status and disease severity. (Watson et al., *supra,* at Ex. 101, p. 4.) Thus, the study demonstrated that the DQB1*0602 allele is not merely associated with type one narcolepsy, it is disease modifying. (*Id*.) The authors therefore concluded that "[r]egardless of the diagnostic utility of HLA genotyping, the presence of HLA-DQB1*0602 likely identified an etiologically distinct and symptomatically more severe narcolepsy phenotype." (*Id*. at 6.) In that regard, Dr. Shafrir's own citations reflect that genetic susceptibility is a "chief pillar" of autoimmunity. (Segal & Shoenfeld, *supra,* at Ex. 85, p. 2; Agmon-Levin et al., *supra,* at Ex. 84, p. 1.) Moreover, Dr. Shafrir agreed during cross-examination that his theory of causation depends specifically on cross-reaction between influenza and hypocretin and that the primary studies he relies upon with respect to that showing were all dependent upon the subjects having the DQB1*0602 allele. (Tr. 108, 130-31; *see also* Luo et al., *supra,* at Ex. 37.) Accordingly, even if HLA-DQB1*0602-positive narcolepsy is not coextensive with type one narcolepsy as Dr. Shafrir asserts (Tr. 215-16), the evidence strongly suggests that it is a distinct etiologic phenotype. Further, on this record, the Pandemrix vaccine has been implicated as a cause of only that specific phenotype. (*See* Vuorela et al., *supra,* at Ex. C, Tab 6.)

This understanding is consistent with Dr. Shafrir's own articulation of the science. Dr. Shafrir specifically stated in his expert report that

> One of the rare cases in which molecular mimicry was demonstrated is in narcolepsy caused by influenza vaccine . . . However, even in the case of narcolepsy and influenza vaccination we are far from understanding the full mechanism. For example, only a tiny minority of the patients who carry the major risk factor of HLA DQB1*06:02/DQA1*01:02 and received the H1N1 vaccine with the offensive adjuvant actually developed narcolepsy.

(Ex. 25, pp. 49-50.)

Regardless of her clinical diagnosis, petitioner's HLA test specifically confirms she is *not* within that HLA-DQB1*0602-positive phenotype of narcolepsy. Therefore, even if Dr. Shafrir's theory vis-à-vis narcolepsy was accepted, the fact that petitioner tested negative for HLA-DQB1*0602 *dramatically* undercuts any application of Dr.

Shafrir's theory of causation to petitioner's own specific case regardless of whether it is dispositive of diagnosis.

Further to this threshold issue, petitioner's medical records do not support her claim that her condition is vaccine caused. On the whole, they reflect a complicated medical history that fails to establish any clear explanation for petitioner's condition. While Dr. Shafrir has many criticisms of petitioner's treating physicians and the healthcare system more broadly, that does not change the nature of the records the treating physicians created or what those records actually evidence.[28] Nonetheless, petitioner argues that her "treating physicians have hypothesized that her conditions are directly related to her October 2105 vaccinations as there is seemingly no logical explanation otherwise." (ECF No. 98, p. 9 (citing Ex. 7, pp. 71, 73).) On this point petitioner cites to Dr. Shehan's record from March 16, 2016. Petitioner is quite right to characterize this as merely hypothesis. Specifically, Dr. Shehan wrote of petitioner: "She has an unusual symptom complex and this may relate to the immunizations. I am going to have to research them a little bit to see if there is anything that makes sense." (Ex. 7, p. 73.) This is the only treating physician notation petitioner presents as providing any support for vaccine causation and it is clearly inadequate to support her burden of proof.

Another special master has previously explained that medical records may include notations where a physician "may well be indicating a *question* in the physician's mind whether there is a causal relationship, or a *suspicion* that there might be a causal relationship. However, that is quite different from an indication that such physician has reached a *conclusion* concerning a causal relationship." *Stapleford v. Sec'y of Health and Human Servs.,* No. 03-234V, 2009 WL 1456441, at *17 n.24 (Fed. Cl. Spec. Mstr. May 1, 2009) (emphasis in original), *aff'd*, 89 Fed. Cl. 456 (2009). In this case, the fact that Dr. Shehan had not reached a conclusion regarding vaccine causation is explicitly confirmed by his statement that he needed to conduct further research "to see if anything makes sense." (Ex. 7, p. 73.) Moreover, the Federal Circuit has explained that "[a]lthough probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." *Althen*, 418 F.3d at 1278 (citing *Grant*, 956 F.2d at 1149). Thus, "[a] treating physician's recognition of a temporal relationship does not advance the analysis of causation." *Isaac v. Sec'y of Health and Human Servs*., 2012 WL 3609993, at *26. Here, even assuming that Dr. Shehan recorded an unequivocal opinion that petitioner's condition was vaccine-related, his opinion as stated would still at best represent recognition that petitioner began experiencing unusual symptoms after her vaccinations.

[28] For example, Dr. Shafrir indicated that he felt petitioner should have been treated with immunotherapy for her chronic fatigue syndrome (Tr 77-79); however, when pressed on cross-examination as to whether that was the standard of care for chronic fatigue syndrome, Dr. Shafrir engaged in extended discussion of what he felt the standard of care should be without ever grappling with what the standard of care actually is for chronic fatigue syndrome. (*Id.* at 116-20.) It should also be noted that Dr. Shafrir's qualification is as a neurologist, which reduces his credibility with respect to his attempts to re-diagnose petitioner with conditions that are not within his area of expertise. (*E.g. Id.* at 120-21.)

Petitioner otherwise relies primarily on Dr. Shafrir's separate diagnostic opinion to make sense of petitioner's clinical history. In that regard, petitioner notes that while Dr. Shafrir has identified several specific diagnoses, he also expressed that petitioner's symptoms "fit very well" the diagnostic criteria for chronic fatigue syndrome. (ECF No. 101, pp. 2-3.) In fact, the viability of this one diagnosis is not disputed by respondent's expert. (Tr. 166.) However, the presence of chronic fatigue syndrome does not help support any logical sequence of cause-and-effect implicating petitioner's vaccinations as a cause of her condition(s). For the reasons discussed above, there is not preponderant evidence either that (a) chronic fatigue syndrome is autoimmune or (b) that, even if so, it is vaccine-triggered. (*See* n.6-10, *supra*.)

Dr. Shafrir also makes much of the idea that petitioner's initial flu-like presentation is causally meaningful. (Ex. 25, p. 51.) He opines this episode is better understood as a systemic vaccine reaction and as part of petitioner's autoimmune process rather than an actual flu-like illness. (*Id.*) However, the literature he cites also makes clear that chronic fatigue syndrome itself often begins with a presentation of flu-like symptoms. (*See* IOM, *supra,* at Ex. 27, p. 15.) Therefore, if petitioner is properly diagnosed with chronic fatigue syndrome as Dr. Shafrir suggests, then this is explanation enough for the abrupt flu-like episode petitioner experienced, implicating neither autoimmunity nor petitioner's vaccinations.

It is also worth noting that Dr. Shafrir stressed during the hearing that his opinion is based at least in part on the onset of all of petitioner's conditions having been simultaneous, characterizing it as "the main basis of my entire argument." (Tr. 131-32.) However, he provided no discussion whatsoever regarding whether it is actually reasonable to opine that molecular mimicry, bystander activation, and epitope spreading would all generate different diseases that would all manifest at the same time.

For all these reasons, petitioner has not preponderantly demonstrated any logical sequence of cause and effect implicating either of her vaccinations as a cause of her condition.

c. *Althen* prong three

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1278. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *mot. for recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Here, for all the reasons discussed in the preceding sections, this case turns on *Althen* prongs one and two and it is therefore not necessary to separately address *Althen* prong three. Because *Althen* prong three coincides with *Althen* prong one, petitioner's inability to meet her burden under prong one effectively precludes her from being able to meet her burden under *Althen* prong three. However, even assuming the timing of petitioner's flu-like episode is generally consistent with molecular mimicry leading to autoimmune injury, it is far from clear that Dr. Shafrir is credible in stressing the simultaneous onset of all of the conditions he has identified for the reasons discussed under Althen prong two, above. But in any event, if petitioner did satisfy *Althen* prong three, that alone would not satisfy her overall burden of proof. *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that a "temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury"); *Hibbard v. Sec'y of Health & Human Servs.*, 698 F.3d 1355, 1364-65 (Fed. Cir. 2012) (holding the special master did not err in resolving the case pursuant to prong two when respondent conceded that petitioner met prong three).

VI. Conclusion

Petitioner has clearly suffered and for that she has my sympathy. The fact that this decision effectively leaves her condition unexplained is in no way meant to minimize her condition or the impact it has had on her life. However, for all the reasons discussed above, petitioner has not met her burden of proof with specific respect to demonstrating that her condition (in whole or in part) was vaccine caused. Accordingly, this case is dismissed.[29]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[29] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.